

## **AMENDMENTS TO THE CLAIMS**

The following listing of claims replaces all prior listings, and all prior versions, of claims in the application.

### **LISTING OF CLAIMS:**

1. (Currently Amended) An automated method for identifying agents that cause a phenotypic change in a cell comprising the steps of:
  - providing receptacles in an array;
  - providing a statistical design including generic factor names, factor levels, and experimental runs;
  - utilizing a software program to generate a computer representation of said statistical design, said computer representation being generated by automatically mapping the identities of agents to said generic factor names, by mapping the concentration or amounts of said agents to said factor levels, and by mapping the locations of said receptacles within said array to said experimental runs;
  - placing different mixtures of single said agents into select ones of said receptacles in said array according to said computer representation of said statistical design;
  - contacting said placed mixtures with said cells;
  - acquiring data indicative of a phenotypic change in said contacted cells;
  - utilizing a processor including an algorithm for comparing said phenotypic data with said statistical design to identify which of said mixtures of single agents and/or ~~or~~ which of said single agents in said mixtures are effective in causing said phenotypic change in said contacted cells; and

storing said statistical design, said agent identities, said computer representation of said statistical design, said acquired data, and the results of said algorithm comparison in one or more databases.

2. (Original) The method of claim 1, wherein a user inputs said identities and said concentrations or amounts of said agents into said software program.
3. (Original) The method of claim 1, wherein a user inputs said statistical design into said software program.
4. (Original) The method of claim 1, further comprising the step of generating a computer program for a robotic system to perform said placing step.
5. (Original) The method of claim 1, further comprising the step of placing single said agents into others of said receptacles in said array.
6. (Original) The method of claim 1, wherein said receptacles includes a surface which is coated with an agent-immobilizing material.
7. (Original) The method of claim 6, further comprising the step of covalently immobilizing said mixtures of single agents to said agent-immobilizing material on said receptacle surface.

8. (Original) The method of claim 6, wherein said agent-immobilizing material is a biocompatible polymer that includes reactive groups for covalently immobilizing said agents.

9. (Original) The method of claim 1, wherein the all of said databases are a single integrated or federated database.

10. (Original) The method of claim 1, wherein the identification of said mixtures that are effective in causing said phenotypic change is determined by fitting statistical models

11. (Original) The method of claim 1, wherein the identification of said mixtures that are effective in causing said phenotypic change is determined by direct comparisons among said mixtures and/or against controls.

12. (Original) The method of claim 1, wherein said processor further includes an algorithm for comparing the performance of said single agents or said mixtures of said single agents over multiple experiments in order determine trends or patterns, wherein said comparisons are stored in a database and can be periodically updated.

13. (Original) The method of claim 1, wherein said statistical design is a fractional factorial design, a d-optimal design, a mixture design, or a Plackett-Burman design.

14. (Original) The method of claim 1, wherein said statistical design is a space-filling design based a coverage criteria, a lattice design, or a latin square design.

15. (Original) The method of claim 1, wherein said agents comprise cellular ligands and/or extrinsic factors.
16. (Original) The method of claim 15, wherein said agents are selected from the group consisting of extracellular matrix proteins, extracellular matrix protein fragments, peptides, growth factors, cytokines and combinations thereof.
17. (Original) The method of claim 1, further comprising repeating said steps with a subset of said identified mixture of single agents.
18. (Original) The method of claim 1, further comprising repeating said steps, wherein the concentrations of single agents in said identified mixture of single agents are varied.
19. (Original) The method of claim 1, further comprising the step of identifying internal cellular mechanisms associated with said phenotypic change.
20. (Original) The method of claim 19, wherein said identifying of cellular mechanisms comprises extracting scientific information on cellular pathways and comparing said extracted information with said identified mixture of single agents and said phenotypic change.
21. (Original) The method of claim 20, wherein said information is computer-extracted.

22. (Original) The method of claim 20, wherein said information comprises gene expression data, protein expression data, cellular phenotype data, signal transduction data, data on cellular pathways, and combinations thereof.

23. (Original) The method of claim 19, wherein said identifying of cellular mechanisms comprises identifying genes and/or proteins expressed by said cells in the presence of said identified mixture of single agents.

24. (Original) The method of claim 19, wherein said identifying of cellular mechanisms comprises identifying which receptors on said cells are activated in the presence of said identified mixture of single agents.

25. (Original) The method of claim 1, wherein said processor further includes a first application program for calculating the likelihood that a cellular pathway, protein, or gene is involved in changes in cellular phenotype associated with said identified mixture of single agents, wherein said cellular pathway or protein is determined using scientific information.

26. (Original) The method of claim 25, wherein said scientific information is selected from the group consisting of gene expression data, protein expression data, cellular phenotype data, signal transduction data, data on cellular pathways, and combinations thereof.

27. (Original) The method of claim 25, wherein said scientific information is stored in one or more databases.

28. (Original) The method of claim 25, wherein said scientific information comprises the identification of genes and/or proteins expressed by said cells in the presence of said identified mixture of single agents.

29. (Original) The method of claim 25, wherein said scientific information comprises the identification of receptors on said cells which are activated in the presence of said identified mixture of single agents.

30. (Currently Amended) The method of claim 1, wherein said phenotypic data is acquired by immunocytochemistry-immunocytochemistry analysis.

31. (Original) The method of claim 30, wherein said immunocytochemistry analysis determines whether biological markers are present that indicate proliferation and/or differentiation of said cells in the presence of a particular mixture of single agents.

32. (Original) A system for identifying agents that cause a phenotypic change in a cell, comprising:

an array of receptacles, selective ones of which are for receiving (i) different mixtures of single said agents, and (ii) fluid including said cells;  
a statistical design including generic factor names, factor levels, and experimental runs;

a software program for generating a computer representation of said statistical design, wherein said software program automatically maps the identities of said agents to said generic factor names, maps the concentration of or amounts of said agents to said factor levels, and maps the locations of said receptacles in said array to said experimental runs;

acquired experimental data indicative of said phenotypic change in said cells;

a processor including an algorithm for comparing said experimental data with said statistical design to identify which of said mixtures of single agents and/or which of said single agents in said mixtures are effective in causing said phenotypic change in said cells; and

one or more databases for storing said statistical design, said agent identities, said computer representation of said statistical design, said acquired experimental data, and the results of said algorithm comparison.

33. (Original) The system of claim 32, wherein said databases are a single integrated or federated database.

34. (Original) The system of claim 32, further comprising a robotic system to place said mixtures of single agents correctly in said receptacles based on said computer representation of said statistical design.

35. (Original) The system of claim 34, further comprising a computer program with instructions for said robotic system to place said mixtures of single agents correctly in said receptacles based on said computer representation of said statistical design.

36. (Currently Amended) The system of claim ~~31~~32, wherein said processor further includes an algorithm for comparing the performance of said single agents or said mixtures of said single agents over multiple experiments in order to determine trends or patterns, wherein said comparisons are stored in a database.